Treatment of Parkinson's Disease & Other Parkinsonian Syndromes

Oluwadamilola O. Ojo MD, FMCP
Associate Professor, CMUL
Consultant Neurologist, LUTH

Nigeria Parkinson's Disease Research Network

International Parkinson and Movement Disorder Society

Disclosures

- None relevant to this talk

Financial conflicts of interest

- None relevant to this talk

Nigeria Parkinson's Disease Research Network

International Parkinson and Movement Disorder Society

Outline

- Diagnostic criteria
- Treatment of motor symptoms of PD
- Treatment of non-motor symptoms of PD
- Early versus advanced disease
- Management of complications
- Management considerations in atypical parkinsonism
- Challenges of management in Africa

Nigeria Parkinson's Disease Research Network

International Parkinson and Movement Disorder Society

Review of the diagnostic criteria

Nigeria Parkinson's Disease Research Network

International Parkinson and Movement Disorder Society

Diagnosis hinges on recognition of *parkinsonism*

UK PD BB CRITERIA

Step 1: Diagnosis of Parkinsonian Syndrome

◆ Bradykinesia (slowness of initiation of voluntary movement with progressive reduction in

speed and amplitude of repetitive actions)

◆ And at least one of the following:

◇ Muscular rigidity

◇ 4–6Hz resting tremor

◇ Postural instability not caused by primary visual, vestibular, cerebellar, or proprioceptive

dysfunction

MDS DIAGNOSTIC CRITERIA

- **I. Criteria for Parkinsonism**
- The prerequisite to apply the MDS-PD criteria is the diagnosis of parkinsonism, which is based on 3 cardinal motor manifestations.

Parkinsonism is defined as bradykinesia, in combination with either rest tremor, rigidity, or both. These features must be clearly demonstrable and not attributable to confounding factor

- **Clinically Established PD OR**
- **Clinically Probable PD**

Nigeria Parkinson's Disease Research Network

International Parkinson and Movement Disorder Society

Diagnosis hinges on recognition of *parkinsonism*

UK PD BB CRITERIA

Step 2: Exclusion Criteria for Parkinson Disease

- History of repeated strokes with stepwise progression of parkinsonian features
- History of repeated head injury
- History of definite encephalitis
- Oculogyric crises
- Neuroleptic treatment at onset of symptoms
- More than one affected relative
- Sustained remission
- Strictly unilateral features after 3 years
- Supranuclear gaze palsy
- Cerebellar signs
- Early severe autonomic involvement
- Early severe dementia with disturbances of memory, language, and praxis
- Babinski sign
- Presence of a cerebral tumor or communicating hydrocephalus on CT scan
- Negative response to large doses of levodopa (if malabsorption excluded)
- MPTP exposure

MDS DIAGNOSTIC CRITERIA

- **Supportive criteria**

Clear and dramatic beneficial response to dopaminergic therapy.

Presence of levodopa-induced dyskinesia

Rest tremor of a limb, documented on clinical examination (*in past, or on current examination)*

The presence of either olfactory loss or cardiac sympathetic denervation on MIBG scintigraphy

Nigeria Parkinson's Disease Research Network

International Parkinson and Movement Disorder Society

Diagnosis hinges on recognition of *parkinsonism*

UK PD BB CRITERIA

Step 2: Exclusion Criteria for Parkinson Disease

- History of repeated strokes with stepwise progression of parkinsonian features
- History of repeated head injury
- History of definite encephalitis
- Oculogyric crises
- Neuroleptic treatment at onset of symptoms
- More than one affected relative
- Sustained remission
- Strictly unilateral features after 3 years
- Supranuclear gaze palsy
- Cerebellar signs
- Early severe autonomic involvement
- Early severe dementia with disturbances of memory, language, and praxis
- Babinski sign
- Presence of a cerebral tumor or communicating hydrocephalus on CT scan
- Negative response to large doses of levodopa (if malabsorption excluded)
- MPTP exposure

MDS DIAGNOSTIC CRITERIA

- **Supportive criteria**

Clear and dramatic beneficial response to dopaminergic therapy.

Presence of levodopa-induced dyskinesia

Rest tremor of a limb, documented on clinical examination (*in past, or on current examination)*

The presence of either olfactory loss or cardiac sympathetic denervation on MIBG scintigraphy

Nigeria Parkinson's Disease Research Network

International Parkinson and Movement Disorder Society

MDS Clinical Diagnostic Criteria Red Flags …

1. Rapid progression of gait impairment requiring regular use of wheelchair within 5 y of onset
2. A complete absence of progression of motor symptoms or signs over 5 or more y unless stability is related to treatment
3. Early bulbar dysfunction: severe dysphonia or dysarthria (speech unintelligible most of the time) or severe dysphagia (requiring soft food, NG tube, or gastrostomy feeding) within first 5 y
4. Inspiratory respiratory dysfunction: either diurnal or nocturnal inspiratory stridor or frequent inspiratory sighs
5. Severe autonomic failure in the first 5 y of disease.
6. Recurrent (>1/y) falls because of impaired balance within 3 y of onset
7. Disproportionate anterocollis (dystonic) or contractures of hand or feet within the first 10 y
8. Absence of any of the common nonmotor features of disease despite 5 y disease duration.
9. Otherwise-unexplained pyramidal tract signs, defined as pyramidal weakness or clear pathologic hyperreflexia (excluding mild reflex asymmetry and isolated extensor plantar response)
10. Bilateral symmetric parkinsonism throughout the disease course

Nigeria Parkinson's Disease Research Network

International Parkinson and Movement Disorder Society

Diagnosis hinges on recognition of *parkinsonism …..& exclusion*

UK PD BB CRITERIA

Step 3: Supportive Criteria for PD

◆ Three or more required for diagnosis of definite PD

- Unilateral onset –
- - Resting tremor - - Progressive disorder
- Persistent asymmetry -
- Excellent response (70–100%) to levodopa
- Severe levodopa-induced chorea ◇ Levodopa response > 5 years
- Clinical course of 10 years or more

MDS DIAGNOSTIC CRITERIA

- **Absolute Exclusion Criteria**

- Unequivocal cerebellar abnormalities on examination
- Downward vertical supranuclear gaze palsy/ slowing of downward vertical saccades
- Diagnosis of probable bvFTD or PPA according to consensus criteria within first 5 y of the disease
- Parkinsonian features restricted to the lower limbs for more than 3 y

Nigeria Parkinson's Disease Research Network

International Parkinson and Movement Disorder Society

Goals of treatment of PD

Nigeria Parkinson's Disease Research Network

International Parkinson and Movement Disorder Society

Goals of pharmacologic treatment of PD

- Improve motor symptoms & improve disability
- Treat NMS
- Improve HRQoL
- Treat motor complications

Nigeria Parkinson's Disease Research Network

International Parkinson and Movement Disorder Society

Available Therapies For Rx Of Motor Symptoms

- Levodopa
- Levodopa plus COMT-i
- MAO-Bi
- Dopamine agonists
- NMDA receptor antagonist

Anticholinergic

Nigeria Parkinson's Disease Research Network

International Parkinson and Movement Disorder Society

MDS COMMISSIONED REVIEWS

International Parkinson and Movement Disorder Society Evidence-Based Medicine Review: Update on Treatments for the Motor Symptoms of Parkinson's Disease

Susan H. Fox, MRCP, PhD,[1,2*] Regina Katzenschlager, MD,[3] Shen-Yang Lim, MD, FRACP,[4] Brandon Barton, MD, MS,[5,6] Rob M. A. de Bie, MD, PhD,[7] Klaus Seppi, MD,[8] Miguel Coelho, MD,[9] Cristina Sampaio, MD, PhD,[10,11] on behalf of the Movement Disorder Society Evidence-Based Medicine Committee

[1]*Edmund J. Safra Program, Movement Disorder Clinic, Toronto Western Hospital, Toronto, Ontario, Canada*
[2]*University of Toronto Department of Medicine, Toronto, Ontario, Canada*
[3]*Department of Neurology and Karl Landsteiner Institute for Neuroimmunological and Neurodegenerative Disorders, Danube Hospital, Vienna, Austria*
[4]*Division of Neurology and the Mah Pooi Soo & Tan Chin Nam Centre for Parkinson's & Related Disorders, University of Malaya, Kuala Lumpur, Malaysia*
[5]*Rush University Medical Center, Chicago, Illinois, USA*
[6]*Jesse Brown VA Medical Center, Chicago, Illinois, USA*
[7]*Department of Neurology, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands*
[8]*Department of Neurology, Medical University Innsbruck, Innsbruck, Austria*
[9]*Department of Neurology, Santa Maria Hospital, Instituto de Medicina Molecular, University of Lisbon, Lisbon, Portugal*
[10]*Cure Huntington's Disease Initiative (CHDI) Management/CHDI Foundation, Princeton, NJ, USA*
[11]*Instituto de Medicina Molecular, University of Lisbon, Lisbon, Portugal*

International Parkinson and Movement Disorder Society

Conclusions from the EBM review ....

- To date, no intervention with efficacy of preventing or slowing PD disease progression.
- There are several options for monotherapy in early PD (levodopa and all DAs significantly improve motor symptoms)
- Non-pharmacologic interventions (gait & balance)
- Enhancing levodopa duration of action using COMT and/or MAO-B inhibition remains an effective approach for reducing motor fluctuations

Nigeria Parkinson's Disease Research Network

International Parkinson and Movement Disorder Society

Treatment of NMS

Nigeria Parkinson's Disease Research Network

International Parkinson and Movement Disorder Society

Evaluation

- **History (clinician review)**
- **MDS non-motor rating scales**
  - **Non-Motor Symptoms Questionnaire (NMSQ)**
    Martinez-Martin P, Schapira AH, Stocchi F, et al. Prevalence of nonmotor symptoms in Parkinson's disease in an international setting; study using nonmotor symptoms questionnaire in 545 patients. Mov Disord 2007;22:1623-1629
    - Chaudhuri KR, Martinez-Martin P, Brown RG, et al. Results from an international pilot study. Mov Disord 2007;22:1901-1911

  - **Non-Motor Symptoms Scale (NMSS)**

    Chaudhuri KR, Martinez-Martin P, Schapira AH, et al. International multicenter pilot study of the first comprehensive self-completed nonmotor symptoms questionnaire for Parkinson's disease: the NMSQuest study. Mov Disord 2006;21:916-923

  - **MDS- NMS**

Nigeria Parkinson's Disease Research Network

International Parkinson and Movement Disorder Society

RESEARCH ARTICLE

The *Movement* Disorder Society Evidence-Based Medicine Review Update: Treatments for the Non-Motor Symptoms of Parkinson's Disease

Klaus Seppi, MD,[1]* Daniel Weintraub, MD,[2] Miguel Coelho, MD,[3] Santiago Perez-Lloret, MD, PhD,[4]
Susan H. Fox, MRCP (UK), PhD,[5] Regina Katzenschlager, MD,[6] Eva-Maria Hametner, MD,[1] Werner Poewe, MD,[1]
Olivier Rascol, MD, PhD,[4] Christopher G. Goetz, MD,[7] and Cristina Sampaio, MD, PhD[8]*

MDS COMMISSIONED REVIEW

Update on Treatments for Nonmotor Symptoms of Parkinson's Disease—An Evidence-Based Medicine Review

Klaus Seppi, MD,[1]* K. Ray Chaudhuri, MD,[2] Miguel Coelho, MD,[3] Susan H. Fox, MRCP (UK), PhD,[4]
Regina Katzenschlager, MD,[5] Santiago Perez Lloret, MD,[6] Daniel Weintraub, MD,[7,8]
Cristina Sampaio, MD, PhD,[9,10]
and the collaborators of the Parkinson's Disease Update on Non-Motor Symptoms Study Group on behalf of the Movement Disorders Society Evidence-Based Medicine Committee

Nigeria Parkinson's Disease Research Network

International Parkinson and Movement Disorder Society

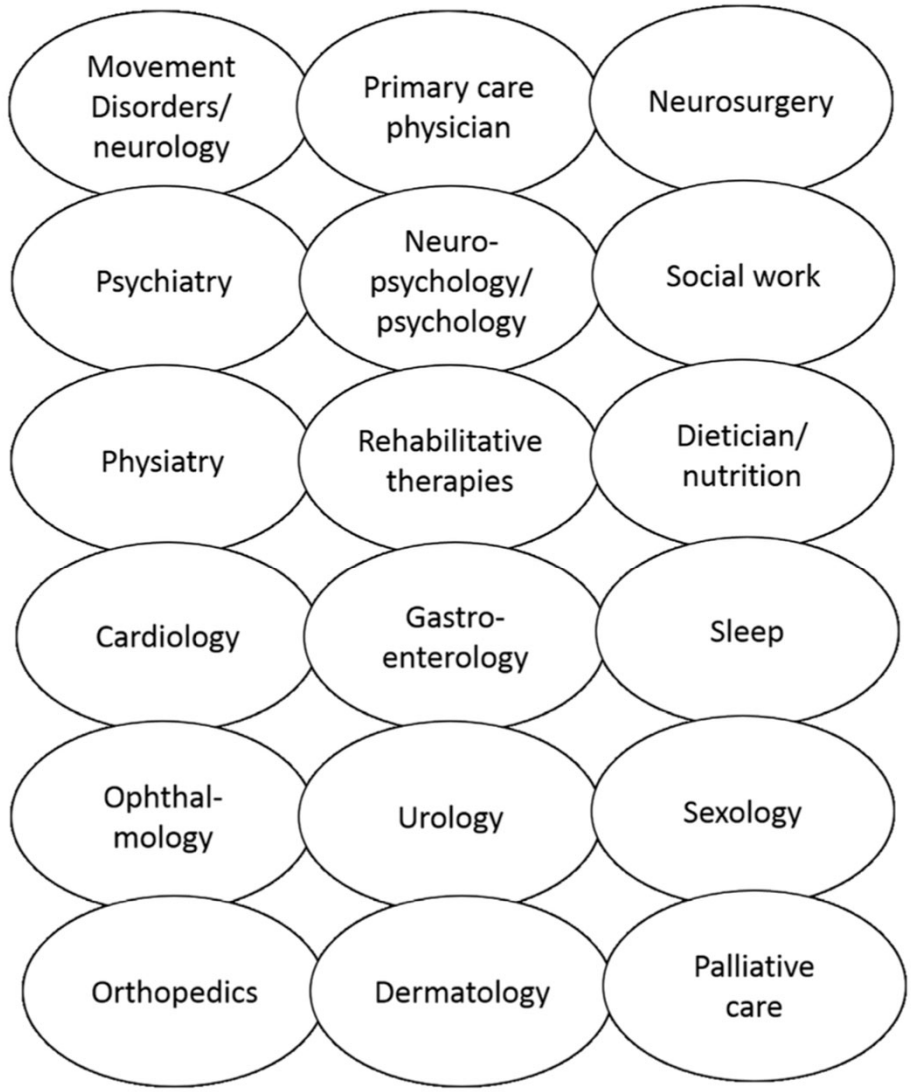

Fig. 1. Multidisciplinary approach to nonmotor symptoms in Parkinson disease: potential team members and specialists.

Goldman JG et al
Neurol. Clinics 2020

Nigeria Parkinson's Disease Research Network

International Parkinson and Movement Disorder Society

Management considerations in atypical parkinsonisms

- Lack (or loss/transient nature) of levodopa responsiveness
- Autonomic dysfunction – measures for postural hypotension, supine hypertension, management of bladder issues
- Postural abnormalities & painful dystonias (BoNT)
- Fall prevention
- Tracheostomy

Nigeria Parkinson's Disease Research Network

International Parkinson and Movement Disorder Society

Challenges of PD Management in Africa

- **Lack of awareness**
- **Delayed diagnosis, delayed access to treatment & care**
- **Lack of caregiver support**
- **Lack of financial support**

Adapted from Six Action Steps to Address Global Disparities in Parkinson Disease: A World Health Organization Priority. JAMA Neurol. 2022;79(9):929-936

Nigeria Parkinson's Disease Research Network

International Parkinson and Movement Disorder Society

Take home messages

- Diagnosis is key! The “spot” diagnosis is a syndrome - parkinsonism NOT PD
- Periodic reviews of the diagnosis is (sometimes) required
- Treatment is lifelong, symptomatic, pays attention to NMS as well as motor symptoms
- Interdisciplinary management is key

Nigeria Parkinson's Disease Research Network

International Parkinson and Movement Disorder Society

Resources/References

- Gibb WR, Lees AJ. The relevance of the Lewy body to the pathogenesis of idiopathic Parkinson's disease. J Neurol Neurosurg Psychiatry. 1988;51(6):745-752. doi:10.1136/jnnp.51.6.745
- Postuma RB, Berg D, Stern M, et al. MDS clinical diagnostic criteria for Parkinson's disease. Mov Disord. 2015;30(12):1591-1601. doi:10.1002/mds.26424
- Pantelyat A. Progressive Supranuclear Palsy and Corticobasal Syndrome. Continuum (Minneap Minn). 2022;28(5):1364-1378. doi:10.1212/CON.0000000000001158
- Fox SH, Katzenschlager R, Lim SY, et al. International Parkinson and movement disorder society evidence-based medicine review: Update on treatments for the motor symptoms of Parkinson's disease [published correction appears in Mov Disord. 2018 Dec;33(12):1992]. Mov Disord. 2018;33(8):1248-1266.

Nigeria Parkinson's Disease Research Network

International Parkinson and Movement Disorder Society

Resources/References

- Katz M. Palliative Care and Movement Disorders. Continuum (Minneap Minn). 2022;28(5):1520-1529. doi:10.1212/CON.0000000000001162
- Greene P. Progressive Supranuclear Palsy, Corticobasal Degeneration, and Multiple System Atrophy. Continuum (Minneap Minn). 2019;25(4):919-935. doi:10.1212/CON.0000000000000751
- Giagkou N, Stamelou M. Therapeutic Management of the Overlapping Syndromes of Atypical Parkinsonism. *CNS Drugs*. 2018;32(9):827-837. doi:10.1007/s40263-018-0551-3
- Seppi K, Weintraub D, Coelho M, et al. The Movement Disorder Society Evidence-Based Medicine Review Update: Treatments for the non-motor symptoms of Parkinson's disease. Mov Disord. 2011;26 Suppl 3(0 3):S42-S80. doi:10.1002/mds.23884

Nigeria Parkinson's Disease Research Network

International Parkinson and Movement Disorder Society